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| 10/016,358 | 10/30/2001 | Richard A. Dixon | SALKINS.017C1 | 6952 |

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KNOBBE MARTENS OLSON & BEAR LLP
2040 MAIN STREET
FOURTEENTH FLOOR
IRVINE, CA 92614

| EXAMINER | |
|---|---|
| IBRAHIM, MEDINA AHMED | |
| **ART UNIT** | **PAPER NUMBER** |
| 1638 | 6 |

DATE MAILED: 11/04/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/016,358 | DIXON ET AL. | |
| | Examiner | Art Unit | |
| | Medina A Ibrahim | 1638 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *21 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *1-19 and 47-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *31 October 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of Group III, claims 20-46, in Paper No. 5, filed on 07/25/03 is acknowledged. The requirement is made FINAL.

2. Claims 1-19 and 47-51, drawn to a non-elected invention have been withdrawn from consideration.

### *Sequence Listing*

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

The sequence Listing filed 10/30/01 has been entered. However, the sequences on page 15, lines 16, and page 43, line 2, have not been identified by SEQ ID NO: Applicant is respectfully requested to identify the sequences presented on pages 15 and 43 or to submit a new Sequence Listing which comprises said sequences. Applicant is also required to amend the specification to include the SEQ ID NO: for said sequences.

### *Drawings*

4. Drawings filed on 10/30/2001 are approved by the Examiner.

### *Claim Rejections - 35 USC § 112*

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 24-26, 31-33 and 39-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Regarding claim 24 and 25, the word "means" is preceded by the word(s) "physical" and "chemical" in an attempt to use a "means" clause to recite a claim element as a means for performing a specified function. However, since no function is specified by the word(s) preceding "means," it is impossible to determine the equivalents of the element, as required by 35 U.S.C. 112, sixth paragraph. See *Ex parte Klumb*, 159 USPQ 694 (Bd. App. 1967). It is suggested that "physical means" and "chemical means" be replaced with , for example, ------microinjection---- and --polyethylene glycol (PEG)----, respectively.

Claims 31-33 are indefinite for depending upon the non-elected claim 5.

Claim 26 is indefinite because "the plant cell" lacks antecedent basis in claim 20. It is suggested that " the plant cell is" be replaced with ---the plant cells are----.

Claim 39 is an incomplete method claim. The claimed method is a method of producing disease resistant plants and comprises the step of introducing a polynucleotide encoding CDR1 polypeptide into the genome of a plant cell to obtain a transformed plant cell. The claimed method lacks a positive step of regenerating a plant from the transformed plant cell. It is also noted that "plants " in the preamble lacks correlation with " a plant cell" in the body of the claims. Dependent claims 40-43 do not

obviate the rejection. Claims 44-46 are included in the rejection because it is unclear if a plant is produced from the method of claim 39.

Claim 41 is indefinite for depending upon the non-elected claim 5.

***Claim Rejections - 35 USC § 112***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 20-31 and 34-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of producing transformed plant and plant cells having resistance against bacterial diseases as result of constitutively expressing SEQ ID NO:1 or a nucleic acid encoding SEQ ID NO:2 and plants/plant cells/seed produced by said method, does not reasonably provide enablement for a method that employs a nucleic acid encoding a constitutive disease resistance (CDR1) polypeptide or a CDR1 promoter inducing amount of an agent to enhance resistance against all diseases in plants. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with these claims.

Applicant broadly claims a method of producing a genetically modified plant having increased disease resistance as compared to its corresponding wild-type plant comprising introducing into plant/plant cells with a nucleic acid encoding a constitutive disease resistance (CDR1) polypeptide, plants produced by said method, and plant tissue and seed derived from said plant. The claims are also drawn to a method of

producing disease resistant plants by contacting susceptible plants with a CDR1 promoter inducing amount of an agent, including a transcriptional factor and a chemical agent, to elevate CDR1 gene expression as compared to a plant not contacted with the agent.

Applicant provides guidance for isolating the nucleic acid of SEQ ID NO: 1 from Arabidopsis by enhancer activation tagging method using T-DNA vectors that contain transcriptional enhancers from the CaMV 35S gene (Examples 1-7). Applicant teaches the antisense expression of SEQ ID NO: 1 under the control of CaMV 35S promoter in wild-type Arabidopsis plants results in transgenic plants that are susceptible to infection by Psuedomonas. Applicant also teaches that increased expression of SEQ ID NO: 1 in transgenic Arabidopsis enhanced resistance against bacterial *Pseudomonas syringe* by inducing expression of PR1 and PR2 genes (Examples 9-10).

*In re Wands (858F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988)* lists a number of factors for determining whether or not undue experimentation would be required by one skilled in the art to make and use the invention. These factors are: the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples of the invention, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Applicant has not provided guidance for the obtention of nucleic acids, other than SEQ ID NO: 1, encoding a constitutive disease resistance (CDR1) polypeptide which can be used for the production of transgenic plants having increased disease

resistance. Neither the instant specification nor the prior art provides evidence that the disclosed activation tagging method can be used for the isolation of CDR1 genes in non-Arabidopsis plants and non-plant organisms. No guidance has been provided with regard to hybridization/wash conditions and/or PCR conditions that will allow specific isolation of the target genes. In the absence of such guidance, undue trial and error experimentation would be required to screen through the vast number of cDNA and genomic clones from other plant and non-plant species, to identify the desired genes.

Bennetzen et al ( Genetic Engineering, Vol. 14, pp. 99-124, 1992(U)) teach identification of disease resistance genes has been largely unsuccessful and may be hampered by large number of genes, by the complexity and size of the plant genome, by the complex and multistep and transient nature of disease resistance, and the lack of direct correlation between chemical substance produced by the plant in response to pathogen attack and actual disease resistance (see page 99, bottom paragraph; page 100, second paragraph; page 102, first full paragraph; page 103, first full paragraph; paragraph bridging pages 103 and 104; paragraph bridging pages 104 and 106; paragraph bridging pages 107 and 108; paragraph bridging pages 109 and 110; page 15, third full paragraph; page 117, bottom paragraph; page 18, second full paragraph). Undue experimentation is required to identify functional resistance homologous genes and evaluate their ability to encode a polypeptide conferring broad-spectrum of disease resistance in plants.

The state of the prior art for modification of gene expression or of a phenotypic characteristics in plants by genetic transformation is highly unpredictable and hence

significant guidance is required to practice the art without undue experimentation. The specific effects of given promoters, leaders, DNA sequences on gene expression in transformed plants can not be anticipated reliably and must be determined empirically (Koziel, et al.; Plant mol. Biol. 32:393-405, 1996, Abstract, pp. 402-403 (W)).

The specification is not enabling for how to identify and use a CDR1 promoter inducing agent and a transcriptional factor to enhance disease resistance in plants, nor that the specification is enabling a method of increasing disease resistance by contacting a susceptible plant with said agents as claimed in claims 34-38. The specification provides no more than an invitation to experiment requiring undue trial and error experimentation.

In *Genentech Inc* v. *Novo Nordisk A/S* (42 USPQ2d 1001 at p. 1005) the court stated "(p)atent protection is granted in return for an enabling disclosure of an invention, not for vague intimidations of general ideas that may or may not workable.... When there is no disclosure of any specific starting material or of any of the conditions under which a process can be carried out, undue experimentation is required....". Applicant is here expecting others to identify transcriptional factors and other CDR1 promoter inducing agents that are not specifically disclosed in the specification, and then determine how to use them to increase resistance against plant diseases and evaluate how broad the range of resistance is.

The specification is enabling only for resistance against bacterial diseases. The claims encompass methods for providing resistance to other plant pathogens including fungi, viruses and nematodes. However, no product is known to confer universal

disease resistance against all plant diseases. For example, Ryals et al (The Plant Cell, vol. 8, pp. 1809-1819, (V)) discuss systematic acquired resistance (SAR) as follows: "In tobacco SAR activation results in a significant reduction of disease symptoms caused by the fungi *Phytophthora parasitica*, *Cercospora nicotiana*, and *peronspora tabacina*, the virus tobacco mosaic virus (TMV) and tobacco necrosis virus..... However, the protection is not effective against all pathogens". For example, there is no significant protection against either *Botrytis cinerea or alternaria alternata*".

When In re Wands factors are weighed it is concluded that undue experimentation would be required to practice the invention throughout the full scope of the claims, and therefore the invention is not enabled.

***Written Description***

9. Claims 20-30, 34-40 and 42-46 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of producing a genetically modified plant having increased disease resistance as compared to the corresponding wild-type plant comprising contacting plant cells by physical and chemical means with a nucleic acid encoding a constitutive disease resistance (CDR1) polypeptide, plants produced by said method, and plant tissues and seed derived from said plant. The claims are also drawn to a method of producing disease resistant plants by contacting susceptible plants with

a CDR1 promoter inducing amount of an agent, including a transcriptional factor and a chemical agent, to elevate CDR1 gene expression as compared to a plant not contacted with the agent.

To satisfy the written description requirement, the specification must describe every element of the claimed invention in sufficient detail so that one of ordinary skill in the art would recognize that the inventor possessed the claimed invention at the time of filing (see vas-Cath, 935 F.3d at 1563; Lockwood v. American Airlines, Inc., 107 F.3d 1565 (Fed. Cir. 1997).

The *University of California v. Eli Lilly and Co.* 43 USPQ2d 1398 (Fed. Cir. 1997) states "A description of a genus of cDNA may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. See also where the court teaches that the disclosure of a process for obtaining cDNA from a particular organism and the description of the encoded protein fail to provide an adequate written description of the actual cDNA from the organism which would encode the protein from that organism, despite the disclosure of a cDNA encoding that protein from another organism.

Applicant describes a method of increasing bacterial disease resistance by introducing into plant/plant cells the nucleic acid sequence of SEQ ID NO: 1, or nucleic acid sequences encoding SEQ ID NO: 2, and plants and plant cells produced by said method, and plant tissues and seed produced from said plant.

Applicant has not described the composition or the structure of other nucleic acids encoding a constitutive disease resistance (CDR1) polypeptide, or a CDR1 promoter inducing agent, or a transcriptional factor for a CDR1 gene expression, which are all necessary to practice the claimed methods. A nucleic acid encoding CDR1 polypeptide is described only by its function or the desired result of its use. Applicant has not described specific chemical, physical, or any other relevant identifying characteristics that distinguish a nucleic acid encoding a constitutive disease resistance (CDR1) polypeptide from other disease resistance genes.

While the specification describes SEQ ID NO:1 from Arabidopsis as an exemplary CDR1 gene, the disclosure of SEQ ID NO: 1 does not provide an adequate written description for the nucleic acid as broadly claimed, from any source, including not just plant but non-plant sources. The specification fails to describe structural features common to all nucleic acids encoding a CDR1 polypeptide that would allow a skilled artisan to predictably determine what will be the identity of the members of the genus. Consequently, the claimed method that employs a nucleic acid encoding a constitutive disease resistance (CDR1) polypeptide is not adequately described.

The specification is silent with regard to the composition or structure of a CDR1 promoter inducing agent and a transcriptional factor for the expression of a CDR1 gene, and a review of literature does not indicate that they are well known to a skilled artisan. Given this lack of written description, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan

would recognize that Applicant was in possession of the invention as broadly claimed at the time of filing.

Therefore, weighing all factors above, the claimed invention does not meet the current written description requirements. See, also Written Description Examination Guidelines published in Federal Registry/Vol. 66, No.4/Friday, January 5, 2001/Notices).

***Claim Rejections - 35 USC § 102***

10. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

11. Claims 20-30, 39-40, and 42-46 are rejected under 35 U.S.C. 102(b) as being anticipated by Ryals et al (US 5,614, 395).

The claims are drawn to a method of producing a genetically modified plant having increased disease resistance as compared to the corresponding wild-type plant comprising contacting plant cells by physical and chemical means with a nucleic acid encoding a constitutive disease resistance 1 (CDR1) polypeptide, plants produced by said method, and plant tissue and seed derived from said plant. The claims also encompass regeneration and selection of disease resistant plants and resistance against *Psuedomonas syringe* bacterial pathogen. Note, neither the specification nor the claims provide limitations that distinguish a nucleic acid encoding a CDR1

polypeptide from prior art nucleic acids encoding polypeptides having constitutive disease resistance activity.

Ryals et al teach a method of producing transformed plants/plant cells having increased resistance against diseases by transforming plant cells with a vector comprising nucleic acid sequences encoding pathogen-related (PR) proteins operably linked to promoters including tissue-specific, constitutive and inducible promoters. PR proteins provide constitutive disease resistance activity against pathogens including bacterial pathogens (columns 7-8 and 18-20). Ryals et al also teach regeneration of plants from said transformed plant cells and selection of transgenic plants with enhanced resistance against pathogens including *Psuedomonas syringe* and transgenic plants and seed and plant tissue from said transgenic plants (Examples 109-175). The reference also teaches transformation by direct gene transfer method including microinjection and use of chemical agent (columns 2 and 3). Resistance to specific strains of *Psuedomonas syringe* of *Pst and Psm* would be an inherent property. All claim limitations are disclosed by the cited reference.

***Remarks***

12. Claims 31-38 and 41 are free of the prior art because the prior art do not teach or suggest a method of increasing disease resistance in a plant with an isolated polynucleotide encoding SEQ ID NO:2, and a method that employs a CDR1 inducing amount necessary to enhance disease resistance of a susceptible plant.

13. Claims 32 and 33 would be allowable if rewritten to overcome the rejection(s) under 35 U.S.C. 112, second paragraph, set forth in this Office action and to include all of the limitations of the base claim and any intervening claims.

14. No claim is allowed.

15. Papers related to this application may be submitted to Technology Sector 1 by facsimile transmission. Papers should be faxed to Crystal Mall 1, Art Unit 1638, using fax number (703) 308-4242. All Technology Sector 1 fax machines are available to receive transmission 24 hrs/day, 7 days/wk. Please note that the faxing of such papers must conform with the Notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Medina A. Ibrahim whose telephone number is (703) 306-5822. The Examiner can normally be reached Monday-Thursday from 8:30AM to 5:30PM and every other Friday from 9:00AM to 5:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Dr. Amy Nelson, can be reached at (703) 306-3218.

Any inquiry of a general nature or relating to the status of this application should be directed to the receptionist whose telephone number is (703) 308-0196.

11/3/03
Mai

Medina A. Ibrahim